REMARKS

A. Status of the Claims and Explanation of the Amendments

Of the 39 claims originally filed in this application, claims 1, 10-12, 15-17, 19-21, 23-27, and 39 have been rejected, while claims 2-9, 13, 14, 18, 22, and 28-38 have been withdrawn. In this paper, Applicants have requested cancellation of claim 21 without prejudice or disclaimer. When this amendment has been entered, the claims under examination will be claims 1, 10-12, 15-17, 19-20, 23-27, and 39.

The Examiner has objected to claims 12 and 15 for minor grammatical errors. These claims have been amended to correct these errors. Thus, Applicants respectfully request reconsideration and withdrawal of the objection to these claims.

Claim 1 has been amended to further clarify the invention. Now claim 1 recites, inter alia, "[a] composition comprising a non-covalent association complex of...a) a positively-charged backbone; and at least two non-identical members selected from the group consisting of...". Support for this amendment is found generally throughout the specification. See, e.g., Figures 1 and 2. A similar amendment has been made for claim 39. Applicants respectfully assert that no new matter has been added by this amendment.

Claim 19 has been amended to include the claim elements of claims 15 and 21. Additionally, claim 19 now recites that the efficiency groups can be "HIV-TAT or fragments thereof". Support for this claim element is found on page 9, line 7 of the specification. No new matter has been added by these amendments.

Claims 10, 19, 20, and 23-27 stand rejected under 35 U.S.C. §112, ¶2 for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

Claim 12 has been rejected under 35 U.S.C. §112, ¶1 for allegedly failing to comply with the written description requirement. The Examiner states that a comma has been added to the claim between the phrases "HIV-TAT" and "and fragments thereof", which "has the effect of rendering the 'and fragments thereof' limitation applicable to both $(gly)_n$-arg-arg-arg-arg-arg-arg-arg and HIV-TAT, whereas previously the claim did not embrace fragments of -$(gly)_n$-arg-arg-arg-arg-arg-arg-arg" [Office Action, page 7]. The inclusion of the extra comma was the result of a typographical error, and was not intended to broaden the scope of the claim. In this response, Applicants have amended the claim to remove the comma in question. Reconsideration and withdrawal of the rejection of claim 12 are respectfully requested.

Claims 19-21 stand rejected under 35 U.S.C. §102(b) as allegedly being anticipated by U.S. Patent No. 5,744,166 to Illum ("Illum"). Claims 1, 11, 12, 19-21, 23, and 24 are currently rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Wu et al. (J. Biol. Chem. 262(10): 4429-4432, 1987) (hereafter, "Wu"), in view of GenBank Accession No. M77788(2005). Claims 1, 11, 12, 19-21, 23, 24, and 27 stand rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Cristiano et al. (Proc. Nat. Acad. Sci. USA 90: 11548-11552) (hereafter "Cristiano"). Claims 1, 11, 12, 19-21, 23-25, and 27 currently stand rejected under 35 U.S.C. §102(a) as allegedly being anticipated by Puls et al. (Gene Therapy 6, 1774-1778, 1999) (hereafter "Puls"), in view of a webpage with a URL of http://www.genlantis.com/catalog/product_line.cfm?product_family_key=13&product_ line_ key=54. Claims 1, 10-12, 19-21, 23, 24, 27, and 39 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Illum, in view of the 1998 Promega catalog. Claims 19, 24, and 26 current stand rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Puls, in view of U.S. Patent No. 6,280,937 to Luo et al. ("Luo"). Finally, claim 39 is rejected under 35 U.S.C.

§103(a) as allegedly being unpatentable over Wu, in view of GenBank Accession No. M77788 (2005).

C. Response to the Rejections Under 35 U.S.C. §112

Applicants respectfully traverse the rejection of claims 10, 19, 20, and 23-27 under 35 U.S.C.§ 112, ¶2 for allegedly being indefinite for failing to point out and distinctly claim the subject matter which applicant regards as the invention.

The Office Action alleges that the term "length" in claim 10 is indefinite because it is not clear what standard should be used to determine length. Previously, Applicants argued that "length" refers to the number of repeating units in a chain, citing page 7 lines 28-32 for support. Here, Applicants further note that Applicants' specification provides a way to measure length. Specifically, on page 7, lines 9-11, the specification explains that "[s]ize to size (**length**) ratios can be determined based on molecular studies of the components or **can be determined from the masses of the components**" (emphasis added). In other words, because the mass of the component is directly related to the number of repeating units in a chain, but not indicative of the straight line distance from one end of the chain to the other end (because the conformation of the chain may vary), one of ordinary skill in the art would understand that "length", as used in Applicants' specification and claims, refers to the number of repeating units of a chain. Thus, the term "length" as used in claim 10 is not indefinite.

Applicants also respectfully assert again that only a single copy of a particular group (b) member should be used to calculate the length of the positively charged backbone as recited in claim 10. Because an individual wishing to practice this invention will select the specific group (b) members of interest, and because these group (b) members have a defined

length (in terms of repeating units in a chain, as discussed above), it is possible for the individual to be able to select a positively charged backbone that has "a length of from about 1 to 4 times the combined lengths of said members from group b)" as recited in claim 10. In other words, the determination of the required length of the positively charged backbone to satisfy the limitations of claim 10 can be done even before the positively charged backbone is mixed with the group (b) members. Thus, the actual amount of the positively charged backbone relative to the actual amount group (b) members in a given mixture is not relevant to the determining whether the length limitation of claim 10 is satisfied, contrary to the statements in the Office Action.

Thus, claim 10 is not indefinite, and the rejection of claim 10 under 35 U.S.C. §112, ¶2 should be withdrawn. Additionally, even though page 4 of the Office Action rejected claims 19, 20 and 23-27 under 35 U.S.C. §112, ¶2 as well, the Office Action did not set forth any specific bases for rejection of these claims. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 19, 20, and 23-27 under 35 U.S.C. §112, ¶2 as well.

D. Response to the Rejections under 35 U.S.C. § 102(b)

1. The § 102(b) Rejection over Illum

Applicants respectfully traverse the rejection of claims 19 and 20 under 35 U.S.C. §102(b) as allegedly being anticipated by Illum. The Examiner had maintained the previous rejection, arguing that

> the Examiner is unable to find in Fig. 1, or in the specification as a whole, any limiting definition of the term "efficiency group". As a result, this term has been given its broadest reasonable interpretation, i.e., any group that is in any way related to efficiency. The PEG group of Illum is considered to be an "efficiency group" because it would reasonably be expected to

> increase the half life of the complex in circulation, thereby increasing the efficiency of the complex.

In response, Applicants respectfully direct the Examiner to Example 3 of the specification, which provides a comparison of the membrane penetration ability of polylysine (MW 150,000 represented by mixture 1) versus polylysine conjugated to a $-Gly_3Arg_7$ group (see mixtures 2-5) for delivering a plasmid expressing blue fluorescent protein. Example 3 clearly shows that the conjugation of the $-Gly_3Arg_7$ group (which is an example of an "efficiency group" as described on page 9, lines 7-10 of the specification) to polylysine leads to more efficient cell membrane penetration and thus greater delivery of the plasmid. Thus, one of ordinary skill in the art, upon reading Applicants' specification (and in particular page 9, lines 7-10 and Example 3) would understand that an "efficiency group" refers to the efficiency of cell membrane penetration ability.

Moreover, Applicants respectfully assert that Illum does not teach, disclose, or suggest the efficiency groups as recited in Applicants' amended claim 19 and corresponding dependent claims. Accordingly, because Illum fails to teach, disclose, or suggest all of the claim elements of claims 19-20, the rejection of these claims under 35 U.S.C. §102(b) as being anticipated by Illum should be withdrawn. MPEP §2131.

2. The § 102(b) Rejection over Wu

Applicants respectfully traverse the rejection of claims 1, 11, 12, 19-20, 23, and 24 under 35 U.S.C. § 102(b) as allegedly being anticipated by Wu, as evidenced by GenBank Accession No. M77788(2005). Briefly, Wu fails to teach, disclose, or suggest all of the claim elements of Applicants' claims. Accordingly, the rejection should be withdrawn.

Previously, Applicants had argued that Wu did not anticipate these claims because Wu only discloses a conjugate between pSV2 CAT and polylysine, whereas Applicants' claim 1 requires at least three components. However, the March 7, 2006 Office Action maintained the §102(b) rejection over Wu, on the basis of the following two interpretations of Wu:

> (1) that group member 'iv' is considered to be the strand of DNA that encodes the selectable marker beta lactamase, and group member 'iii' is considered to be the complementary DNA strand; and
>
> (2) distinct plasmids are considered to be two members, since each plasmid comprises both DNA, and DNA encoding a persistence factor.

Applicant respectfully disagrees with the Office Action's characterization of Wu. With respect to the Office Action's first interpretation, it appears that the Office Action has taken the position that the strand of DNA that encodes the selectable marker beta lactamase is one "member" whereas the complementary strand is a second "member". However, Applicants respectfully assert that one of ordinary skill in the art would understand the term "DNA", as recited in Applicants' claim 1, to refer to hybridized, double stranded DNA, (i.e., not single stranded), because single stranded DNA does not exist stably in nature. Thus, the Office Action's attempt to arrive at Applicant's invention by reading the term "DNA" to include single strands of DNA of a plasmid as separate "members" is unwarranted and improper. If, however, the Examiner decides to maintain this rejection, Applicants respectfully request the Examiner to take official notice that the term "DNA", without further specification (e.g., as "single stranded DNA") , is known by one of ordinary skill in the art to embrace both single and double stranded DNA and to provide a corresponding reference to support that interpretation.

With respect to the second interpretation, namely, that distinct plasmids can be separate "members", Applicants respectfully note that claim 1 has been amended such that it

now reads ""[a] composition comprising a non-covalent association complex of...a) a positively-charged backbone; and at least two non-identical members selected from the group consisting of...". Thus, because two pSV2-CAT plasmids attached to a polylysine group are not "two non-identical members" as recited in claim 1, this second interpretation of Wu cannot be a basis for arguing that Wu anticipates Applicants' claim 1 and corresponding dependent claims.

Thus, Wu does not teach all of the elements of Applicants' claims 1, 11, 12, 19-20, 23, and 24.

Moreover, the Office Action argues that the asialoglycoprotein recited in Wu is an "efficiency group" because (1) "Applicant has failed to point to any limiting definition in the specification of the term "efficiency group" and (2) asialoglycoproteins, which the Office Action admits are targeting ligands, "allow complexes to be taken up into cells by receptor mediated endocytosis"...that results in "an increase in uptake efficiency of the complex by the targeted cells" [Office Action, page 12]. Applicants respectfully disagree on both counts. First, as noted above in connection with the discussion of Illum, one of ordinary skill in the art would know from reading Applicant's specification that an "efficiency group" enhances cell membrane penetration [see page 9 of the specification and Example 3 of the specification, for example]. Thus, the term "efficiency group" is not an ill-defined term as alleged on page 12 of the Office Action.

Moreover, Applicants respectfully assert that a targeting ligand as disclosed in Wu merely improves binding specificity, not overall penetration through a cell membrane. Applicants respectfully take the position that the Office Action's reliance on Figure 3 of Wu is misplaced, because this Figure does not illustrate increased cell membrane penetration, only improved specificity towards the target genes from using ASOR-polylysine conjugate.

Applicant still does not see where Wu shows an increased cell membrane penetration by conjugating ASOR to polylysine. At best, it appears to Applicants that Wu only claims increased targeting capability. For example, Wu states "[w]e conclude that asialoglycoprotein-poly-L-lysine conjugates can be used to target genes in a soluble form resulting in specific delivery to hepatocytes and expression of foreign genes by these cells" [Wu, page 4431, second column, second full paragraph]. This does not, in and of itself, show that there was an enhancement in the penetration of the cell membrane.

Additionally, Applicants do not see where Wu teaches the efficiency groups as recited in amended claim 19.

For at least these reasons, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1, 11, 12, 19-21, 23, and 24 under 35 U.S.C. § 102(b) as being anticipated by Wu, in view of GenBank Accession No. M77788(2005).

3. The §102(b) rejection over Cristiano

Applicants respectfully traverse the rejection of claims 1, 11, 12, 19-21, 23, 24, and 27 under 35 U.S.C. §102(b) as allegedly being anticipated by Cristiano. As in its discussion of Wu, the Office Action argues that Cristiano teaches that targeting ligands (e.g., adenovirus and asialoorosomucoid) can be conjugated to a polylysine, and that the targeting ligands are "efficiency groups". The Office Action also argues that the complementary strands of the plasmid DNA can be viewed as separate "members" as recited in claim 1 and the corresponding dependent claims.

Applicants respectfully disagree with the Office Action's assertions, for substantially the same reasons as set forth in Applicants' discussion of the Wu reference. First,

one of ordinary skill in the art would understand the term "DNA", as recited in Applicants' claim 1 to refer to hybridized, double stranded DNA, (i.e., not single stranded), because single stranded DNA does not exist stably in nature. Thus, just as in its discussion of Wu, the Office Action's attempt to arrive at Applicant's invention by reading the term "DNA" to include single strands of DNA of a plasmid as separate "members" is unwarranted and improper. Again, if Examiner decides to maintain this rejection, Applicants respectfully request the Examiner to take official notice that the term "DNA", without further specification (e.g., as "single stranded DNA") , is known by one of ordinary skill in the art to embrace both single and double stranded DNA and to provide a corresponding reference to support that interpretation.

With respect to claim 19 and its corresponding dependent claims, Applicants do not see where Cristiano teaches the efficiency groups as recited in amended claim 19. Moreover, Applicants strongly disagree with the Examiner's position that any two tandem lysines on the polylysine discussed by Cristiano can be considered to be efficiency groups corresponding to an HIV-TAT domain. While poly-amino acids, such as polylysine, have side chains, these side chains are structurally distinct from the conjugated branching groups as described on page 9 of Applicants' specification. Moreover, the Office Action has not established that two tandem lysines can even function at all as an efficiency group (i.e., by promoting penetration of cell membranes). Thus, Applicants respectfully assert that Cristiano fails to teach all of the claim elements of Applicant's claims, and the rejection of Applicants' claims under 35 U.S.C. §102(b) as being anticipated by Cristiano should be withdrawn.

4. The §102(a) Rejection over Puls

Applicants respectfully traverse the rejection of claims 1, 11, 12, 19-20, 23-25 and 27 as allegedly being anticipated by Puls, as evidenced by the genlantis URL. As in the discussion of Wu, Applicants disagree with Office Action's view that the double stranded DNA of the plasmid corresponds to two "members", because one of ordinary skill in the art would consider the term "DNA", without further specification, to refer to double-stranded, hybridized DNA, not single stranded DNA. Thus, Puls does not teach all of the claim elements of Applicant's claim 1 or corresponding dependent claims. Moreover, the antibody targeting ligand is not an "efficiency group" as recited in Applicants' amended claim 19. Additionally, the Office Action's assertion that polylysine can also be a source of positively charged branching groups is incorrect, because Applicants' specification defines branching groups to be structurally different from the lysine side chains present in polylysine.

Accordingly, Applicants respectfully request the reconsideration and withdrawal of the rejection of claims 1, 11, 12, 19-20, 23-25 and 27 over Puls.

D. Response to Rejections Under 35 U.S.C. §103(a)

1. Applicants' Claims Are Patentable Over the Illum, In view of the 1988 Promega Catalog.

Applicants respectfully traverse the rejection of claim 1, 10-12, 19-20, 23, 24, 27 and 29 as allegedly being unpatentable over Illum, in view of the 1998 Promega catalog. Briefly, the combination of references fails to teach, disclose, or suggest all of the claim elements of Applicants' claims. Accordingly, the rejection should be withdrawn.

Applicants' amended claim 1 recites, inter alia, "[a] composition comprising a non-covalent association complex of...a positively-charged backbone; and.. at least two non-

identical members...". Applicants do not see where Illum teaches a positively charged backbone and at least two non-identical members as recited in Applicant's claim 1 and corresponding dependent claims. At best, it appears that Illum merely discusses complexing a polycationic polymer to a single pharmacologically active agent [see abstract].

Moreover, Applicants respectfully assert that the side chains found in polylysine are structurally distinct from the positively charged branching groups as recited in Applicants' claims and discussed on page 9 of Applicants' specification. Thus, Illum fails to teach an efficiency group as recited in claim 19 and corresponding dependent claims.

The 1998 Promega catalog does not appear to alleviate these deficiencies of Illum. Accordingly, Applicants respectfully assert that claims 1, 10-12, 19-20, 23, 24, 27 and 29 are patentable over Illum, in view of the 1998 Promega catalog. Reconsideration and withdrawal of the rejection of these claims under 35 U.S.C. §103(a) are respectfully requested.

2. Applicants' Claims Are Patentable Over Puls, In View of Luo

Applicants respectfully traverse the rejection of claims 19, 24, and 26 under 35 U.S.C. §103(a) as allegedly being unpatentable over Puls, in view of Luo and the genlantis URL.

As noted above, Puls fails to teach, disclose, or suggest an "efficiency group" as recited in amended claim 19.

Luo and the genlantis URL do not alleviate these deficiencies of Puls. Luo is directed to shuttle vectors, such as shuttle vectors that can be expressed in mammalian cells, but can be replicated in at least yeast [See Luo, abstract]. The Office Action does not rely on Luo to cure the deficiencies of Puls, but instead merely relies on Luo for a nucleic acid encoding blue fluorescent protein, as discussed at column 6, lines 45-57 of Luo.

The combination of Puls, Luo, and the genlantis URL does not appear to teach, disclose, or suggest tthe "efficiency group" recited in Applicants' claim 19, and corresponding dependent claims 24 and 26. Because the combination of references fails to teach, disclose, or suggest all of the claimed elements, the rejection should be withdrawn. See MPEP §2143.

3. Claim 39 is Patentable Over the Cited References

Applicants respectfully traverse the rejection of claim 39 as allegedly being unpatentable over Wu, in view of GenBank Accession No. M77788(2005). For substantially the same reasons as set forth in the discussion of the §102(b) rejection over Wu, Applicants respectfully assert that Wu, in view of GenBank Accession No. M77788(2005) fails to teach or disclose all of the claim elements of Applicants' claim 39. Accordingly, the rejection should be withdrawn. MPEP §2143.

CONCLUSION

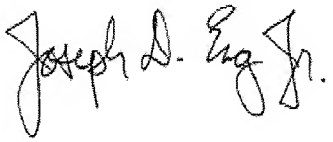
Based on the foregoing amendments and remarks, Applicants respectfully request reconsideration and withdrawal of the rejection of claims and allowance of this application.

AUTHORIZATION

The Commissioner is hereby authorized to charge any additional fees which may be required for consideration of this Amendment to Deposit Account No. **13-4500**, Order No. 4649-4006US1. In the event that an extension of time is required, or which may be required in addition to that requested in a petition for an extension of time, the Commissioner is requested to grant a petition for that extension of time which is required to make this response timely and is hereby authorized to charge any fee for such an extension of time or credit any overpayment for an extension of time to Deposit Account No. **13-4500**, Order No. 4649-4006US1. A DUPLICATE OF THIS DOCUMENT IS ATTACHED.

Respectfully submitted,
MORGAN & FINNEGAN, L.L.P.

Dated: September 7, 2006 By:



Joseph D. Eng Jr.
Registration No. 54,084

Correspondence Address:
MORGAN & FINNEGAN, L.L.P.
3 World Financial Center
New York, NY 10281-2101
(212) 415-8700 Telephone
(212) 415-8701 Facsimile